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EXAMINER	
LEVY, NEIL S	
ART UNIT	PAPER NUMBER
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Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No. 09/991,579	Applicant(s) CHUNG ET AL.
	Examiner McLeay	Group Art Unit 1616 / 27

—The MAILING DATE of this communication appears on the cover sheet beneath the correspondence address—

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, such period shall, by default, expire SIX (6) MONTHS from the mailing date of this communication .
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).

Status

☒ Responsive to communication(s) filed on 4/22/03.

☐ This action is **FINAL.**

☐ Since this application is in condition for allowance except for formal matters, **prosecution as to the merits is closed** in accordance with the practice under *Ex parte Quayle,* 1935 C.D. 1 1; 453 O.G. 213.

Disp sition of Claims

☒ Claim(s) 1-42 is/are pending in the application.

Of the above claim(s) 21-42 is/are withdrawn from consideration.

☐ Claim(s) _____ is/are allowed.

☒ Claim(s) 1-20 is/are rejected.

☐ Claim(s) _____ is/are objected to.

☒ Claim(s) 1-42 are subject to restriction or election requirement.

Applicati n Papers

☐ See the attached Notice of Draftsperson's Patent Drawing Review, PTO-948.

☐ The proposed drawing correction, filed on _____ is ☐ approved ☐ disapproved.

☐ The drawing(s) filed on _____ is/are objected to by the Examiner.

☐ The specification is objected to by the Examiner.

☐ The oath or declaration is objected to by the Examiner.

Pri rity under 35 U.S.C. § 119 (a)-(d)

☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 11 9(a)-(d).

☐ All ☐ Some* ☐ None of the CERTIFIED copies of the priority documents have been

☐ received.

☐ received in Application No. (Series Code/Serial Number) _____.

☐ received in this national stage application from the International Bureau (PCT Rule 1 7.2(a)).

*Certified copies not received: _____.

Attachment(s)

☐ Information Disclosure Statement(s), PTO-1449, Paper No(s). _____

☒ Notice of Reference(s) Cited, PTO-892

☐ Notice of Draftsperson's Patent Drawing Review, PTO-948

☐ Interview Summary, PTO-413

☐ Notice of Informal Patent Application, PTO-152

☐ Other _____

Offic Action Summary

Why is this case identified (top of each page of brief) as 09/260,221?

In view of the brief filed on 4/22/03, PROSECUTION IS HEREBY REOPENED. New grounds of rejection are set forth below.

To avoid abandonment of the application, appellant must exercise one of the following two options:

(1) file a reply under 37 CFR 1.111 (if this Office action is non-final) or a reply under 37 CFR 1.113 (if this Office action is final); or,

(2) request reinstatement of the appeal.

If reinstatement of the appeal is requested, such request must be accompanied by a supplemental appeal brief, but no new amendments, affidavits (37 CFR 1.130, 1.131 or 1.132) or other evidence are permitted. See 37 CFR 1.193(b)(2).

Please note the brief appendix incorrectly recites claim 1 as comprising (i) an- formulation "comprising consisting"-. The claim 1 as last amended, is free of this problem.

Claims 21-42 stand withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected invention, there being no allowable generic or linking claim. Applicant timely traversed the restriction (election) requirement in Paper No. 3.

We note that this case contains a declaration indicating provisional application of 11/4/98, not claimed and not mentioned after the title on p.1 of the specification, therefore not afforded priority.

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Claims 8, 11, 12, 19, 20 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

The claim is indefinite, as reciting "said anabolic agent" when there are 2, precludes knowing which one is intended. There is no estradiol benzoate in claim 1, so no proper antecedent for this compound at claim 8. Likewise with Testosterone propionate, trenbolone, somatotrophin, salts, and derivatives thereof. The claim fails to further limit claim 1. At claim 19; 1-8% is not evident as the % of the dual composition in the specification, but the claim does not specify which or, if both, are referred to. Likewise with claim 20; does the claim refer to immediate, controlled, or both?

Claims 1-20 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for multiple formulations, does not reasonably provide enablement for there is no disclosure of a composition of an immediate release and controlled release agent(s). The dual formulation is not a composition as the term is normally used, but rather dual compositions, more correctly, multiple compositions. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make the invention commensurate in scope with these claims. The specification discloses the invention only in examples as to how to arrive at dual formulations as a method: one puts a controlled release composition, a tablet, with one or more immediate release compositions, tablets.

The ratios of claims 2-4 are not evident in the specification-we do not know, if the ratio is to the separate pellets, as of example 2, to separate total formulations (i) and (ii) or to 2 separate amounts of active. The same is true of claims 11, 12; basis for these is methods described in the specification, not described as a single implant.

Applicants terms are all ... functional, not time described, except as to 28 days equivalent to immediate. The cooperates, is seen as not supported-the term is used, but only zeranol alone is exemplified, and "cooperates" is only a presumption- the superior gain of 4% (533 versus 511 # at 140 days) is possibly the result of 247% more zeranol administered (72g Ralgo versus 178g of the dual formulation).

Finally Hudson and Schaff show when ESTRADIOL is used, a coated implant, or one of the instant formulation (Schaff, Table II) is undesirable if an immediate release occurs. Thus, only specific anabolic implant combinations of which only zeranol is taught would be useful.

Claims 1, 5, 7, 8, 9, 10 are rejected under 35 U.S.C. 102(b) as anticipated by or, in the alternative, under 35 U.S.C. 103(a) as obvious over O'callaghan et al '86.

Sub Q cattle pellets, implantable, consisted of estrdiol and progesterone, estradiol, estradiol and trenbolone acetate, in 15 pellets (col.2, materials-p.427). The formulations, although not labeled as immediate and controlled release, meet the claimed invention. The compounds, as used in all the devices as presented, are known to immediately release the actives. The problem of concern is that of sustained release, effective lifespan varied from 90-120 days (p.427, 2nd ¶). Silastic was known to extend activity to 365 days, providing long acting, slow release, we would equate this effect

with the instant term controlled release, and the instant controlled release agent, as silastic. In comparison, the instant term, "immediate" absent any identification of a specific time period associated with "immediate", is seen as anything less than the long acting, slow release-again both forms known by the artisan, to begin to release active immediately upon insertion in the body. Progesterone is also shown as a controlled – release agent (discussion, ¶ 2, p.429). Trenbolone acetate can readily be envisioned as the instant "immediate release" as it is in a carrier not of the estradiol controlled release silastic (p.428, ¶ 2, treatment (4) on p. 427). Although the instant claim is to a composition, in fact the disclosure is to multiple compositions, not part of the same composition, but are stated to be as a method, administered as an "implant" by simultaneous or successive administration. O'Callaghan so administers (4), p.427) an anabolic implant dual formulation composition as is the instant invention as claimed, when "composition" is not restricted to one unitary product, immediate release is not limited to. Only 1 formulation, or to any time frame, immediate and controlled release are not exclusive terms. Controlled release does not exclude immediate release, and does not exclude slow or continued release. Dual refers to immediate and controlled functions, not to the number of formulations (the instant disclosure provides (example 2) multiple pellets. Cooperation was seen (p.428) when slow (controlled) release silicone estradiol implant was combined with Trenbolone acetate-increase in daily gain. O'callaghan states that zeranol, in the compressed pellet (the O'callaghan controlled release form) was known to be implanted with Trenbolone acetate (the O'callaghan immediate release form), thus, instant claim 9 is met, as is 10 ((4) p.427).

Claims 1,20 are rejected under 35 U.S.C. 103(a) as being unpatentable over O'callaghan et al '86 in view of Nessel et al 3920806 stevens et al 5874098 and Dick et al GB 2167662 O'callaghan (above) provides the instant dual formulations, but does not describe the excipients, diluents, bulking agents etc., as they are implicitly present in the use of commercially avoidable and known implants of silastic, compressed pellets at p.427. Nessel shows one of these forms, stated to be a conventional lactose vehicle (col.2, lines 35-37) and shows that the lactose form provides over 2 times the release rate, even as early as 2 weeks (Table 1) over the polymer containing the instant derivative (claim 8) anabolic agent. Note, however, the Nessel polymers released 100% by 8 weeks; the problem O'callaghan attempts to solve, with extension to 52 weeks.

It would have been obvious to a person of ordinary skill in the art at the time the invention was made desiring to utilize an implant for growth enhancement on cattle, to choose the combination of O'callaghan, as it provides in combination, enhanced effects over single formulations. The particular delivery forms are shown as art recognized, but in detail, were not described. Nessel shows, in the anabolic implant field lactose formulations are known, and known, and provide for immediate release, while polymer forms provide controlled release, the polymer prolonging release to 8 weeks only.

Stevens is cited to show implantation of multiple pellets (fig 1, 2) sub Q to cattle ear is well known, but it was also evident that the concept of an immediate release (quick release) and controlled, sustained release was (example) also known at the time of the instant invention. Stevens does show means of control of time of release (col.5,

top and lines 43-56) by using additives, along with one or more pellets of one or more drugs, including growth hormone. These additives and excipients include lactose, ethylcellulose, binders, and coloring agents. Example 2 shows or compression pellet, of progesterone and estradiol as of O'callaghan. The fast release in this case was not an anabolic agent, however examples show controlled release to be attained by increasing the ratio and amount of active to that of Kamei (formula III and IV, or by using different actives (formula I and II).

Thus, were one to wish to have a biodegradable, implant of the O'callaghan type, it would have been obvious and within the purview of one in the implantation arts to utilize the Stevens ingredients, adjusting the pellets in terms of ratios of quick to controlled release, when the same active is desired, or to choose an immediately releasable compound, such as of Stevens or Trenbolone acetate of O'callaghan, with a controlled release formulation, such as the estradiol/progesterone examples, in order to achieve enhanced results as shown attainable by Callaghan, without the need at the time of Callaghan, of retained implant at slaughter (p.429, discussion). The ratio of polymer to active is shown as 8% (formula I , II , IV of Steven). Immediate to controlled release pellets are disclosed as 1 to 8 (col.5, lines 37-40). Thus, attainment of the benefits of a biodegradable polymer, as opposed to silastic, would be obvious for one in the art to choose in order to reduce inflammation as shown associated with the silastics, utilize the required amount of initial or immediate release anabolic agent, such as Trenbolone acetate of O'callaghan, or b GH and otherwise optimize selection of anabolic agent compound and amount in order to provide less objectionable pressure of

hormone at slaughter, in accord with public desire of for meat free additive, especially hormone.

Dick et al shows the residue problem was known (p.1, lines 17-31) and that prolonged delivery was not. Anabolic agents are of instant-zeranol, trestosterone, estradiol (p.1 lines 59-65) with one, or more than one agent effective, with ratios of 1:10 best.

Claims 1-5, 7-9, 13-15, 20 are rejected under 35 U.S.C. 103(b) as being unpatentable over Ivy et al 4670949 in view of admission in the instant specificaiton. See example 1-an anabolic dual formulation composition, as of the instant invention (p.5, lines 6-90 comprising an immediate release first formulation consisting essentially of (example 1) somatotropin (b GH) and (instant claim 8) RALGRO implanted sub Q-zeranol ((col.5) top) controlled release long acting anabolic agent (col.3, lines 47-51) with a controlled release agent, lactose, as identified in the instant specification as a RALGRO component. Table 5 shows ADG increased in treated versus control (O) animals. So the 2 dosage forms cooperate to effect stimulation.

The instant invention in general, is shown by Ivy, but the specific incorporation of claim 1 compounds is not. See above; Ivy uses zeranol, and somatotrophin, but instant claim 8 expands claim 1 to include somatotrophin, or derivatives of the listed anabolic agents. In this mode, Ivy provides the mix, at the ratios of instant claims 2-4 (col.4, lines 6-19) when zeranol is 200-600 and b GH @ 100.

Implantation (instant claim 5) is sub Q in cattle (column 3, last ¶) alternatively, b GH is identified as long acting col.3, line 66-line 2, col.4, with beeswax or peanut oil controlled release agent (col.4, lines 25-29).

The RALGRO is known to include excipient, lactose as of instant and is stated to be the instant immediate release form, thus meeting instant claims 13-15, 20. Instant claims 2-4 ratios then are met when zeranolis 200 (lines 6-9, col.4) while b GH is 600 (lines 14, 15, col.4).

Ivy presents the instant invention as it is claimed; questionably anticipated, with explanation of Ralgro required in order to recognize the ingredients in addition to zeranol. Since Ivy presents data on a shorter term (weekly) than the instant disclosure (28 days) the terms immediate and controlled can be seen as met by either implant, b GH or Ralgro, or both, the instant language not being mutually exclusive.

Claims 1-9, 11-13, 16, 17, 20 are rejected under 35 U.S.C. 102(b) as anticipated by or, in the alternative, under 35 U.S.C. 103(a) as obvious over Deasy 4874612.

Single implantation of multiple compositions is disclosed (lines 40-50, col.3) of the instant anabolic agents; using PLGA (examples) (a). Implant Ⅱ, 9 pieces, contain 4 controlled-release agents: blank tablets. We see the formulation exemplified provide both immediate and sustained release (Tables Ⅰ, Ⅱ). These examples show the same compositions. However, they are examples; release is within the control of the artisan (col.2, lines 26-58). Clearly, instant release occurs (1 day increase in blood level, Table 2) sustained release occurs, through 90 days test. The instant claims do not define controlled, or immediate, nor does the specification, except to indicate a 28- day

measure, for both immediate or controlled release. The same effects are seen by Deasy, but times are 1, 2, 7, 14-90 days. Cooperation clearly occurred; weight gain over control resulted whether the blank insinuated forms (II) or straight (I) implants was used (Table 3). The same agent estradiol, was used in each shaped piece I the example, but combinations are disclosed, inclusive of zeranol, thus obvious to use as is known in the art, and stated by Deasy, to enhance growth (col.3, lines 30-55). The parameters of control are only different in terms of the example, from the instant invention estradiol rather than RALGRO, no differences between instant as claimed and Deasy are seen in the claimed composition. Diluent/fillers are at col.3, lines 9-15. The ratio of lactide to glycolide is one means of controlling rate of release, and is within the instant ratios (col.5, lines 50-55) of claims 2-4.

Claims 1-13, 16, 17, 19 are rejected under 35 U.S.C. 102(b) as anticipated by or, in the alternative, under 35 U.S.C. 103(a) as obvious over Lewis-5288496.

Lewis provides the invention as it is claimed. See example 11 microparticles of Trenbolone acetate of PLGA are injected, in ear implants, into cattle. This is the instant invention. The release agent is carboxymethylcellulose. The ratio of 30% to 50% PLGA was 1:1. Example 9 uses 4 to 1 blend of estradiol controlled release forms to immediate release forms. Lewis explains how to achieve multiphasic release patterns; the instant controlled and immediate release are seen by manipulating parameters of importance: % loading, use of particular polymers-biodegradable/bioerodable of selected molecular weight, with diffusion release (col.3, line 65-col.4, line 41). The instant growth stimulants are also used (col.3, lines 48-55). Selection of the particular

parameters and values are a function of the amount and particular agent, species of animal, desired treatment period, desired amount of growth promotion, age (col.6, lines 28-47).

Specific examples of specific agents as growth promotes, with different ratios of immediate and controlled release mixes, as are instantly designated, are presented.

Instant claim 11 is suggested, as zeranol is used, the examples are not limited (col.6, last ¶), so it would be either within the confines of the disclosure, or obvious to utilize zeranol, for example, at example 11, instead of Trenbolone acetate. Further, it would be likewise obvious to use 2 or more growth promoters, because they are identified as a small group simply or in combination (col.3, lines 48-55, col.6, lines 42-47). Growth promoter can be as high as 95%, thus, inclusive of instant claim 12. Diluents include oils (col.5) top).

Claims 1-6, 8, 13-16, 19, 20 are rejected under 35 U.S.C. 102(b) as being anticipated by Sivaramakrishnan et al 5219572.

The instant Anabolic dual formulation implant composition, comprising in the instant open guise, at least one undefined immediate release formulation, and at least one, undefined controlled release formulation of Anabolic agents listed in claims 1 and 8, is already known-see claim 1-a plurality of beads of non-uniform rupture times of (claim 4) somatotropin, of as much as 70% of the bead (claim 6) the instant consisting essentially of anabolic agent-see col.4, lines 44-52; somatotropin is the protein. Inclusive of instant claim 19 ratios, are controlled release agents esters, waxes to modify the shells (col.5, lines 16-39) and capsule material (claim 11, and col.5, lines 39-

52) these include hydroxypropylmethyl cellulose, excipients, binders include sucrose (col.6, lines 53-58), the instant diluent (instant claims 13,14). Immediate delivery in 1-6 hours is shown (col.6, lines 46-50) continuing over 14 days. This formulation is in the outer capsule, and up to 70% somatotropin (col.6, lines 41-43).

Underlying controlled release pellets then contain somatotropin also at 40 to 70% (lines 43-45) example 9 show 1 to 6 ratio of immediate to controlled release. The instant lactose is at example 8. The instant implants, as claimed, are met, no patentable weight given to unspecified timeperiods or agents, or interactions-cooperation.

Applicant's arguments filed 4/23/03 have been fully considered but they are not persuasive. Applicants arguments in the brief have been considered, but in light of the claim language are not convincing. Re structured rejection of Lewis, in view of new rejections and considerations under 35 USC 112 has been entered, along with additional rejections based on of the claim language, and also in consideration of the invention as disclosed in essence, the use of 2 compositions as a method is evident as the disclosed invention.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Bernard Dentz whose telephone number is 308-4544. The examiner can normally be reached on Monday-Friday 8 am-4:30 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Allan Rotman can be reached on 308-4698. The fax phone numbers for the

organization where this application or proceeding is assigned are 305-3592 for regular communications and 305-3592 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 308-1235.

Levy/tgd
July 8, 2003

NEIL S. LEVY
PRIMARY EXAMINER